

Correlation of Vitamin B12 Status, Glycemic Control, and Metabolic Profile with Nerve Conduction Velocity in Type 2 Diabetes Mellitus

Authors:

Monazzah Fatima^{1*}, S Aijaz A Rizvi¹, Anwar H Siddiqui¹, Hamid Ashraf²

¹Department of Physiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India.

²Rajiv Gandhi Centre for Diabetes and Endocrinology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India.

*Corresponding Author:

Monazzah Fatima, Department of Physiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India. Email: serenemedico10@gmail.com

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ABSTRACT

Introduction: The neurological consequences of type 2 diabetes mellitus develops insidiously, with abnormalities in peripheral nerve function preceding the appearance of overt clinical symptoms. Nerve conduction studies provide an objective, quantifiable measure of peripheral nerve function that may detect nerve dysfunction before symptoms appear. This study examined how vitamin B12, glycemic control, and lipid profile relate to nerve conduction velocity in patients with type 2 diabetes. **Methods:** Patients with and without type 2 diabetes were recruited in a cross-sectional study. Anthropometric data, fasting lipid profile, glycated haemoglobin, serum vitamin B12, and nerve conduction velocity were recorded for all participants, and Pearson correlation coefficients were calculated between nerve conduction velocity and each biochemical parameter. **Results:** Patients with diabetes had significantly higher body mass index, poorer glycemic control, lower serum vitamin B12, a more atherogenic lipid profile, and slower sural nerve conduction velocity than controls. Nerve conduction velocity correlated positively with vitamin B12 and negatively with glycated haemoglobin, triglycerides, very-low-density lipoprotein, and total cholesterol, while high-density and low-density lipoprotein showed no significant correlation. **Discussion:** Glycemic control showed the strongest association with nerve conduction, followed by vitamin B12 and triglyceride-rich lipoproteins, supporting a model in which hyperglycaemia, dyslipidemia, and B12 status act together, rather than glycaemia alone, to influence peripheral nerve function. **Conclusion:** Assessing vitamin B12 status and lipid profile alongside glycated haemoglobin may help identify patients with type 2 diabetes at greater risk of nerve dysfunction and highlights additional, correctable targets for preserving nerve function, over and above glycemic control alone.

Keywords: Type 2 diabetes mellitus, diabetic peripheral neuropathy, nerve conduction velocity, vitamin B12, dyslipidemia.

INTRODUCTION

Type 2 diabetes mellitus is the fastest growing global health concern in the world. It is estimated that 11.1% of the global adult population, are currently living with diabetes, with more than 90% classified as type 2 diabetes mellitus, and this figure is projected to rise to 853 million by 2050 (1). Diabetic peripheral neuropathy is the most frequent microvascular complication of diabetes, affecting a large proportion of patients over the

course of their disease, and is the leading cause of foot ulceration and non-traumatic lower-limb amputation (2). Nerve conduction studies occupy a central place in the assessment of diabetic peripheral neuropathy. Unlike symptom-based questionnaires or clinical scoring systems, which depend on subjective reporting and can be influenced by pain thresholds, mood, and comorbidities, nerve conduction studies provide an objective, quantifiable, and reproducible measure of peripheral nerve function (3,4). Because nerve

conduction studies may register slowing of conduction well before a patient becomes symptomatic, they allow neuropathy to be identified at a stage when the nerve injury may still be less, rather than only after irreversible axonal loss and clinically overt sensory deficits have developed (5).

A further reason to look beyond glycemic control alone is that several of the factors associated with nerve dysfunction in type 2 diabetes are modifiable. Unlike fixed risk factors such as age, sex, or duration of diabetes, elevated triglycerides and other components of lipid profile can be improved through dietary change, weight loss, exercise, and lipid-lowering therapy (6), while low vitamin B12, which is common in patients on long-term metformin therapy, can be corrected simply and inexpensively through supplementation (7). Because these factors are amenable to intervention, identifying which biochemical parameters most strongly track with nerve conduction abnormalities has direct practical value, it points clinicians toward additional, correctable targets for slowing or preventing the progression of diabetic peripheral neuropathy, over and above glycemic control alone.

Considering these backgrounds, the present study was undertaken to characterize the biochemical profile of patients with type 2 diabetes, and to determine which of these modifiable parameters correlates most strongly with sural nerve conduction velocity, with a view to inform earlier detection and more comprehensive risk-factor management in this population.

RESULTS

Demographic characteristics

Cases and controls were comparable in age (p = 0.187). Residence and educational attainment were broadly similar between groups (Table 1).

Table 1. Demographic characteristics of study participants.

Parameter	Control (n = 30)	Case (n = 30)
Age (years)	45.72 ± 3.23	47.04 ± 4.35
	p-value: 0.1873	
BMI (kg/m²)	22.62 ± 4.97	27.00 ± 6.26
	p-value: 0.004*	
Gender, n (%)		
Male	19 (63.3)	10 (33.3)
Female	11 (36.7)	20 (66.7)
Residence, n (%)		
Urban	18 (60.0)	14 (46.7)
Rural	12 (40.0)	16 (53.3)
Education, n (%)		
Below class 10 th	4 (13.3)	8 (26.7)
Class 10 th	5 (16.7)	10 (33.3)
Class 12 th	9 (30.0)	7 (23.3)
Graduate or above	12 (40.0)	5 (16.7)

MATERIALS AND METHODS

This cross-sectional study included thirty patients with a diagnosis of type 2 diabetes mellitus (cases) and thirty individuals without diabetes (controls). Informed consent was obtained from all participants, and the study was approved by the institutional ethics committee. Age, gender, place of residence (urban/rural), and educational attainment were recorded for all participants. Height and weight were measured, and body mass index was calculated. Venous blood samples were collected after an overnight fast of at least eight hours. Fasting lipid profile (triglycerides, total cholesterol, HDL, LDL, and VLDL), HbA1c, serum vitamin B12 were estimated. Sensory nerve conduction velocity of the sural nerve was recorded bilaterally using standard surface-electrode electroneuromyography technique using using a NeuroStim4 NCV system (Medicaid Systems, Chandigarh, India).

Statistical Analysis

GraphPad Prism 11.0 (GraphPad Software, Boston, Massachusetts, USA) was used for the statistical analysis. Continuous variables are expressed as mean ± standard deviation and were compared between cases and controls using the unpaired t-test. Pearson correlation coefficients (r) were calculated between sural nerve conduction velocity and each biochemical parameter (HbA1c, triglycerides, total cholesterol, HDL, LDL, VLDL, and vitamin B12). A p-value < 0.05 was considered statistically significant.

Biochemical and electrophysiological findings

Cases had higher HbA1c than controls ($8.00 \pm 1.43\%$ vs $5.15 \pm 0.32\%$, $p = 0.0001$). Serum vitamin B12 was significantly lower in cases (427.35 ± 200.92 pg/mL) than in controls (610.24 ± 115.32 pg/mL, $p < 0.0001$). Cases also showed a significantly more atherogenic lipid profile, with higher triglycerides, total cholesterol, LDL, and VLDL ($p < 0.05$ for all four), while HDL did not differ significantly between groups ($p = 0.826$). Sural nerve conduction velocity was significantly slower in cases than controls (38.38 ± 7.08 vs 50.79 ± 5.53 m/s, $p = 0.0001$) (Table 2).

Table 2. Comparison of biochemical and electrophysiological parameters between cases and controls.

Parameter	Control (n=30)	Case (n=30)	p-value
Vitamin B12 (pg/mL)	610.24 ± 115.32	427.35 ± 200.92	$< 0.0001^*$
Triglycerides (mg/dL)	115.83 ± 28.11	202.57 ± 66.68	0.0001^*
Total cholesterol (mg/dL)	152.05 ± 24.08	185.80 ± 50.10	0.0180^*
HDL-cholesterol (mg/dL)	34.99 ± 8.03	34.51 ± 6.28	0.8257
LDL-cholesterol (mg/dL)	87.63 ± 19.94	111.23 ± 32.22	0.0130^*
VLDL-cholesterol (mg/dL)	22.69 ± 4.98	37.00 ± 11.97	0.0001^*
HbA1c (%)	5.15 ± 0.32	8.00 ± 1.43	0.0001^*
Sural nerve conduction velocity (m/s)	50.79 ± 5.53	38.38 ± 7.08	0.0001^*

Correlation of sural nerve conduction velocity with biochemical parameters

Sural nerve conduction velocity correlated negatively with HbA1c ($r = -0.644$, $p = 0.0001$), triglycerides ($r = -0.536$, $p = 0.0023$), VLDL ($r = -0.521$, $p = 0.0032$), and total cholesterol ($r = -0.410$, $p = 0.0243$), and positively with vitamin B12 ($r = 0.582$, $p = 0.0007$). HDL ($r = 0.058$, $p = 0.763$) and LDL ($r = -0.240$, $p = 0.202$) were not significantly correlated with conduction velocity (Table 3).

Table 3. Correlation of sural nerve conduction velocity with biochemical parameters.

Variable pair	r	p-value
HbA1c and sural nerve conduction velocity	-0.644	0.0001^*
Triglycerides and sural nerve conduction velocity	-0.536	0.0023^*
Total cholesterol and sural nerve conduction velocity	-0.410	0.0243^*
HDL and sural nerve conduction velocity	0.058	0.7626
LDL and sural nerve conduction velocity	-0.240	0.2019
VLDL and sural nerve conduction velocity	-0.521	0.0032^*
Vitamin B12 and sural nerve conduction velocity	0.582	0.0007^*

DISCUSSION

Cases and controls were well matched for age, making it unlikely that age confounded the biochemical or electrophysiological differences observed. Regarding place of residence, the distribution was relatively similar between the groups. Urban residents constituted sixty percent of the control group and forty-six percent of the

case group, while rural residents constituted forty percent and fifty-three percent, respectively.

Although the case group showed a somewhat greater proportion of rural participants, the overall distribution did not indicate a marked imbalance between the groups. Educational status showed a tendency toward lower educational attainment in the case group. Conversely, a greater proportion of cases had education at or below the

secondary level. Educational status may reflect differences in health literacy, awareness, healthcare-seeking behaviour, and access to health-related information. The significantly higher BMI in cases is consistent with the well-established link between adiposity, insulin resistance, and the development of type 2 diabetes, and adiposity itself has been implicated as an independent contributor to peripheral nerve dysfunction in diabetic cohorts, alongside hyperglycemia and dyslipidemia (8).

The lower vitamin B12 in cases is consistent with reports that metformin, the first-line oral agent for type 2 diabetes, impairs uptake of the intrinsic factor-B12 complex by ileal cubilin receptors, reducing B12 absorption in an estimated 10-30% of long-term users, and that low B12 status is common among patients with type 2 diabetes and is associated with a worse neuropathy profile (9). Cases had significantly higher triglyceride, total cholesterol, LDL cholesterol, and VLDL cholesterol concentrations than controls, whereas HDL cholesterol was comparable between the groups. The prominent elevation of triglycerides and VLDL, together with increased LDL and total cholesterol, indicates a more adverse lipid profile among cases. Dyslipidemia may contribute to peripheral nerve dysfunction through metabolic and vascular mechanisms, including oxidative stress, endothelial dysfunction, and impairment of the microvascular supply to peripheral nerves (2,8). The absence of a significant difference in HDL cholesterol suggests that the lipid alterations in this cohort may be driven predominantly by elevations in atherogenic and triglyceride-rich lipoproteins. The coexistence of poorer glycemic control and an adverse lipid profile in the case group suggests the presence of multiple metabolic factors that may contribute to peripheral nerve dysfunction.

The strong inverse correlation between HbA1c and sural nerve conduction velocity observed here is consistent with findings from several nerve conduction studies in type 2 diabetes. Electrophysiological studies have shown that elevated HbA1c is associated with significant deterioration in peroneal, tibial, and sural nerve conduction velocities, and that HbA1c variability over time is independently associated with the severity of peripheral neuropathy, including reduced sural sensory nerve conduction velocity, reinforcing HbA1c as a key modifiable determinant of nerve function in diabetes (10). The correlation of triglycerides and VLDL with slower nerve conduction adds to the growing body of evidence implicating dyslipidemia, independent of glycemia, in nerve fiber injury.

The positive correlation between vitamin B12 and sural nerve conduction velocity is consistent with reports that patients with type 2 diabetes and neuropathy have lower

B12 levels and worse neuropathy profiles than those with adequate B12 status (11). Researchers have reported that B12 repletion can improve electrophysiological and autonomic measures of diabetic neuropathy, supporting a modifiable role for B12 status in nerve dysfunction, particularly in patients on long-term metformin therapy (12).

Together, the correlation pattern observed in this study, strongest for HbA1c and vitamin B12, and moderate for triglycerides and VLDL, is compatible with a model in which hyperglycemia may exert the dominant effect on large myelinated fiber conduction, while dyslipidemia and B12 deficiency may act as secondary but still statistically significant contributors.

Strengths of the Study

The present study has several strengths. First, the study assessed multiple potentially modifiable metabolic factors, including glycemic control, vitamin B12 status, and lipid profile, rather than focusing on glycemic control alone. Second, sural nerve conduction velocity was assessed using an objective electrophysiological measure, providing a quantitative assessment of peripheral nerve function. Finally, the correlation analysis helped identify the relative strength and direction of associations between biochemical parameters and nerve conduction velocity.

Limitations of the Study

This study has certain limitations. First, the sample size was relatively small, which may limit the statistical power and generalizability of the findings. Second, the cross-sectional design permits identification of associations but does not establish a causal relationship between vitamin B12 status, glycemic control, lipid abnormalities, and nerve conduction velocity. Finally, the study was conducted in a single institutional setting, and therefore the findings may not be directly generalizable to all populations with type 2 diabetes mellitus.

Future Research and Clinical Implications

Future studies should include larger and more diverse populations and preferably use prospective, multicentre designs to confirm the associations observed in the present study. Longitudinal studies would be particularly valuable for determining whether improvement in glycemic control, correction of vitamin B12 deficiency, and management of dyslipidemia can slow or reverse deterioration in nerve conduction. Interventional studies assessing the effect of vitamin B12 supplementation and optimized metabolic management on electrophysiological parameters may further clarify whether these potentially modifiable factors have a direct therapeutic role in diabetic peripheral neuropathy.

CONCLUSION

Assessing vitamin B12 status and lipid profile alongside glycated haemoglobin can help identify patients with type 2 diabetes who are at greater risk of nerve dysfunction, even when glycemic control is the dominant factor. Incorporating these routinely available and correctable parameters into risk assessment, rather than relying on glycemic control alone, offers a practical and low-cost way to identify patients who may benefit from closer monitoring or earlier intervention to preserve peripheral nerve function, and this approach warrants confirmation in larger, prospective, multicentre studies.

Declarations

Ethics Approval

The study protocol was reviewed and approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh-202002, India (Approval No. IEC/JNMC/1405; approval date: 20 April 2024).

Consent to Participate

Informed consent was obtained from all participants prior to enrolment in the study.

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The authors declare that no specific funding was received for this study.

Conflict of Interest

The authors declare that they have no conflict of interest related to this study.

Authors' Contributions

Monazzah Fatima: Conceptualization, methodology, data collection, statistical analysis, interpretation of results, and original manuscript preparation. S Aijaz A Rizvi: Study supervision, conceptualization, resources, and manuscript review and editing. Anwar H Siddiqui: Project administration and editing. Hamid Ashraf: Clinical supervision and revision of the manuscript.

All authors reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Data Availability Statement

All datasets for this study are available from the corresponding author on reasonable request.

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